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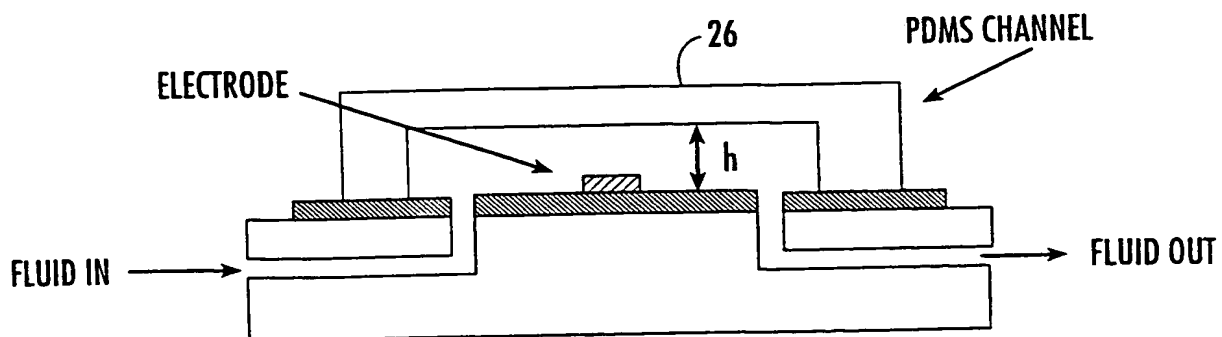
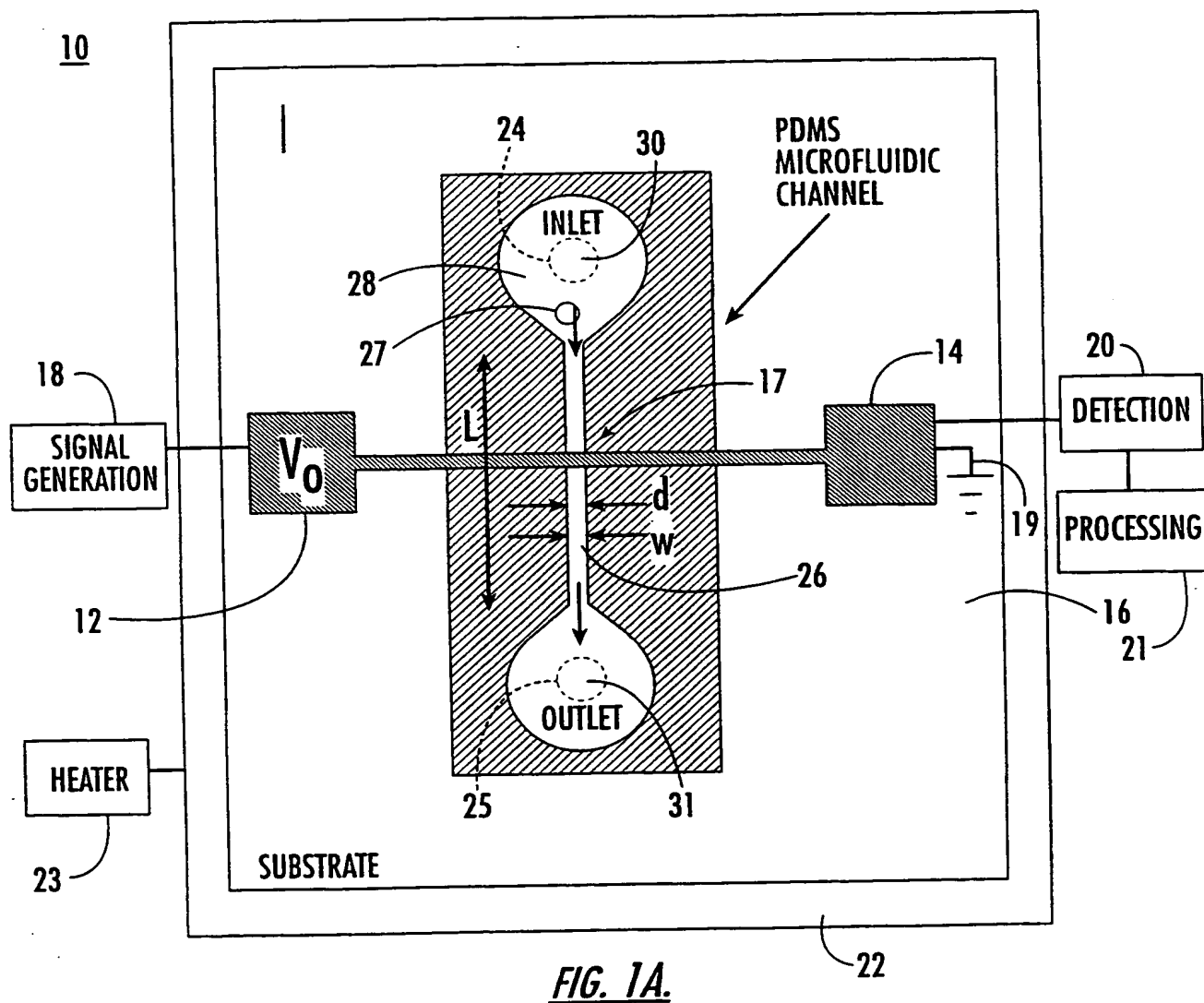
- (51) International Patent Classification⁷: **C12Q 1/68**,
G01N 33/53, C12M 1/00, 1/42, C07H 21/02, 21/00, B01L
3/00
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- (84) Designated States (regional): European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).
- Published:**
— With international search report.
— Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: MICROFLUIDIC AND NANOFUIDIC ELECTRONIC DEVICES FOR DETECTING CHANGES IN CAPACITANCE OF FLUIDS AND METHODS OF USING

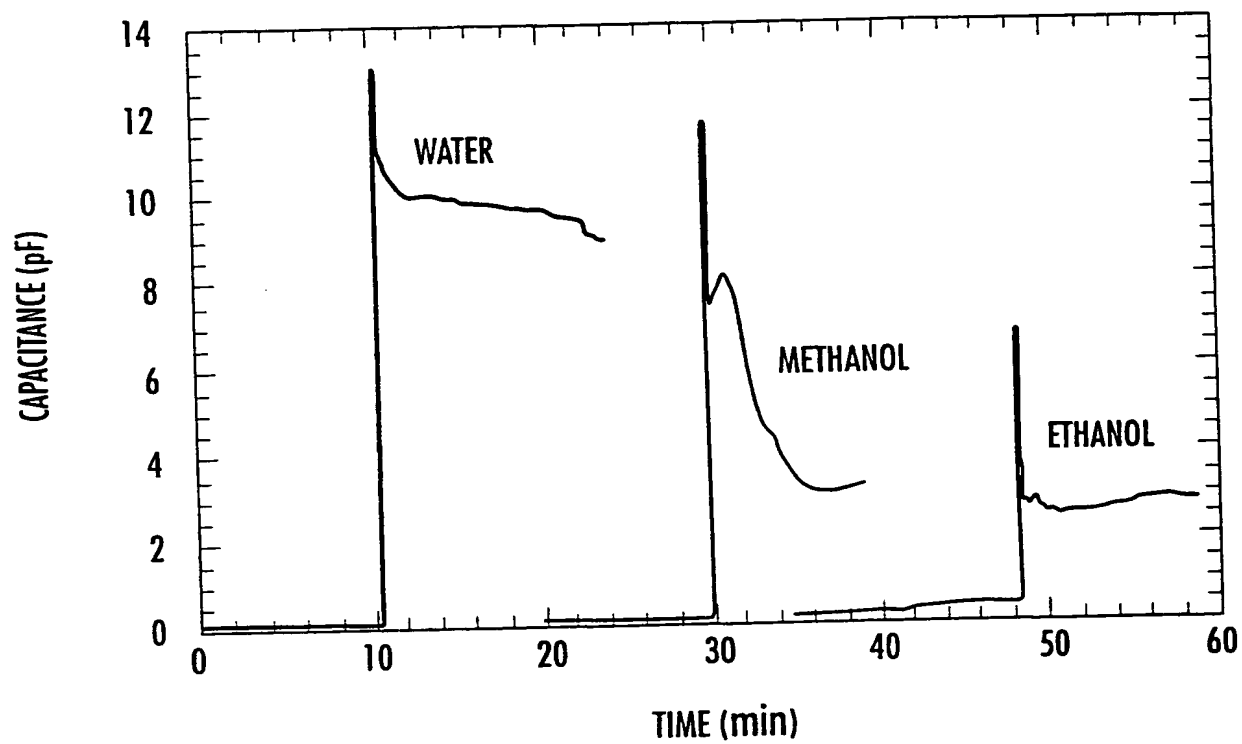
(57) Abstract: The present invention relates to microfluidic and nanofluidic devices for detecting or measuring an electrical property of a fluid including a liquid or aerosol, a single molecule or a single particle or cell in a fluid. In a particular embodiment, the devices detect or measure changes in capacitance of a fluid, molecule, particle or cell as it passes through the device. The present invention also relates to the detection and measurement of single molecules, in particular, biological molecules. The present invention also relates to methods of sequencing polynucleotide molecules, such as RNA or DNA, by detecting differentially labeled single nucleotides. Applications of this technology of single molecule detection, includes DNA or RNA sequencing which require a resolution of 3-5 nucleotides, detection of SNPs which require a single nucleotide resolution, proteomics which require 3 nucleotide resolution, and particle sizing. The microfluidic device can be used to determine the DNA content of cell, to analyze cell-cycles kinetics of populations of cells and as an assay for abnormal changes in DNA content of cells. The nano-microfluidic devices of this invention also have utility for use as detectors in molecular sorting systems and detecting of pathogens and spores. The present invention is also referred to as "Capacitance cytometry".

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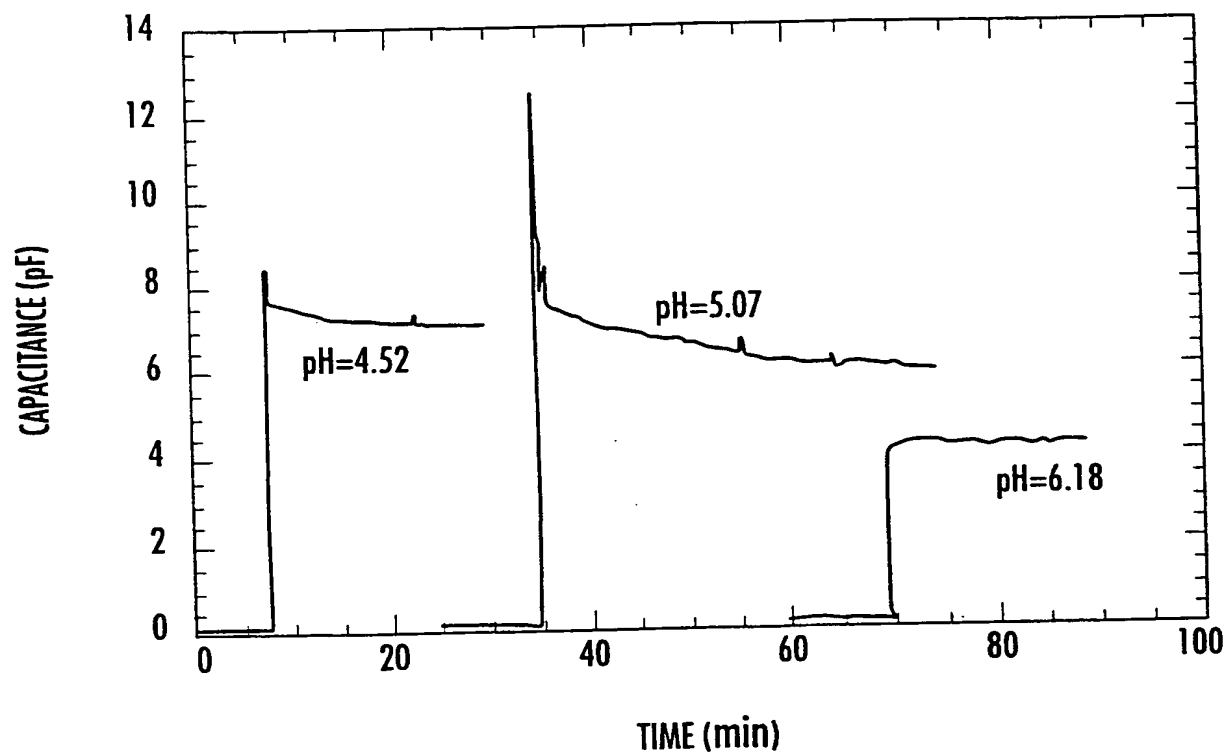
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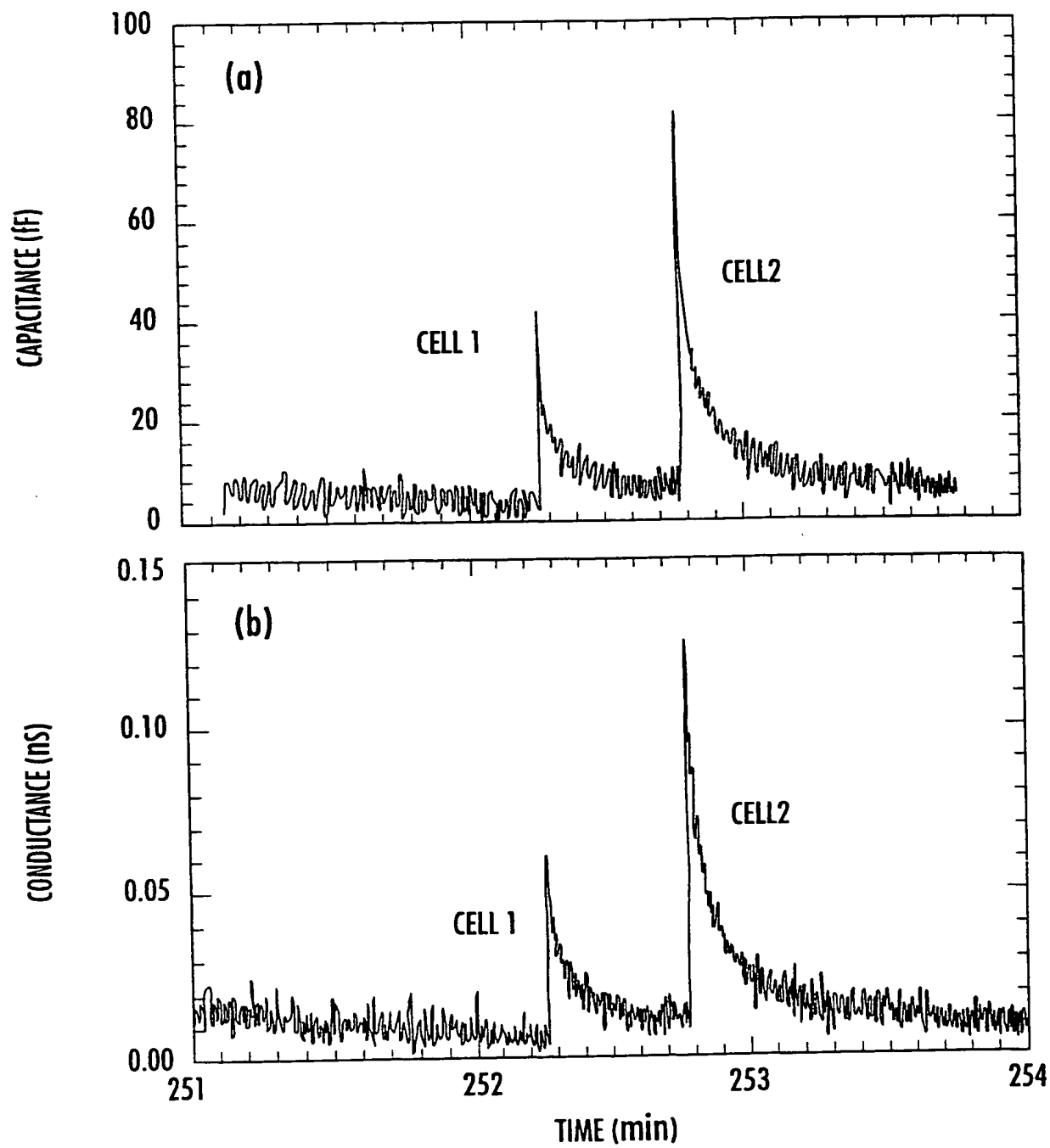
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FIG. 2.

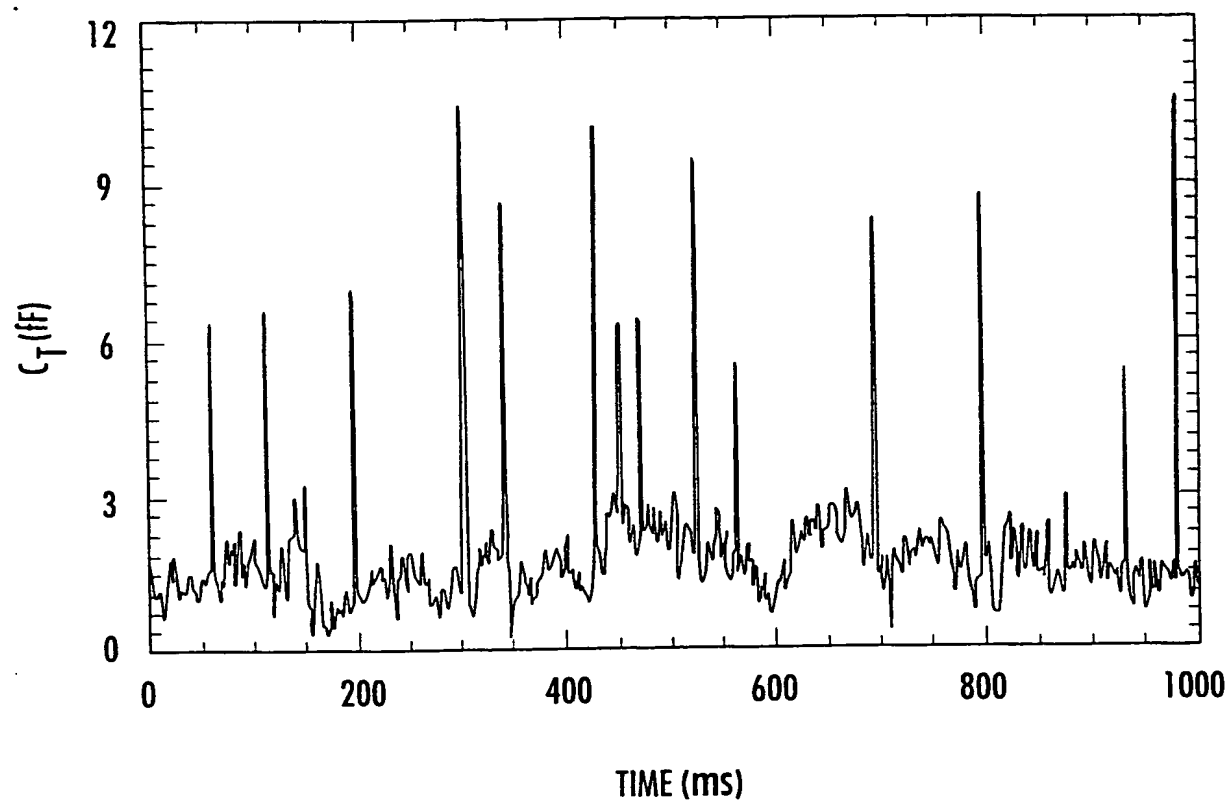
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FIG. 3.

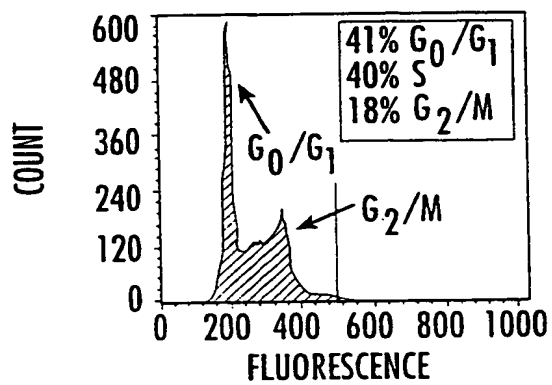
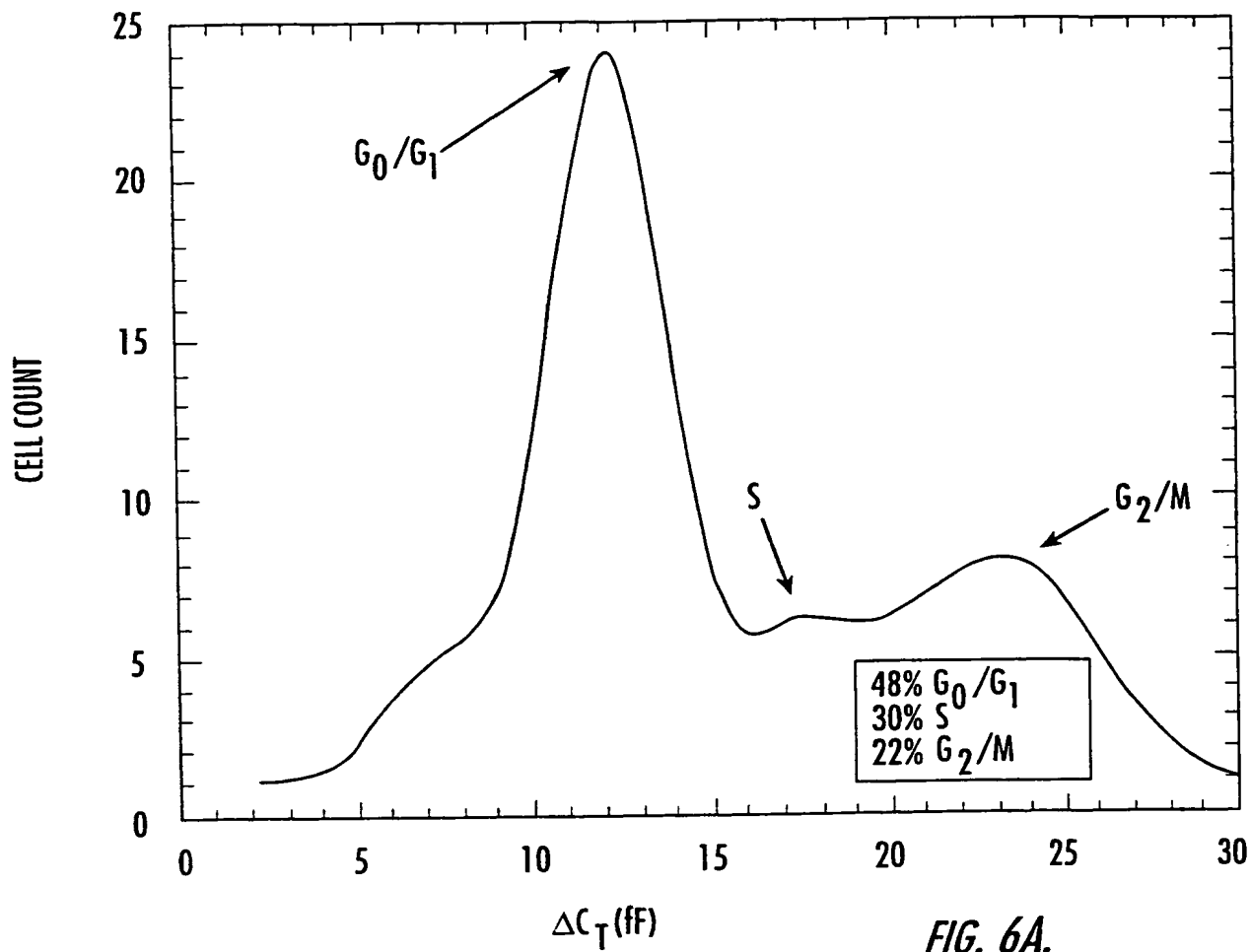
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**FIG. 4.**

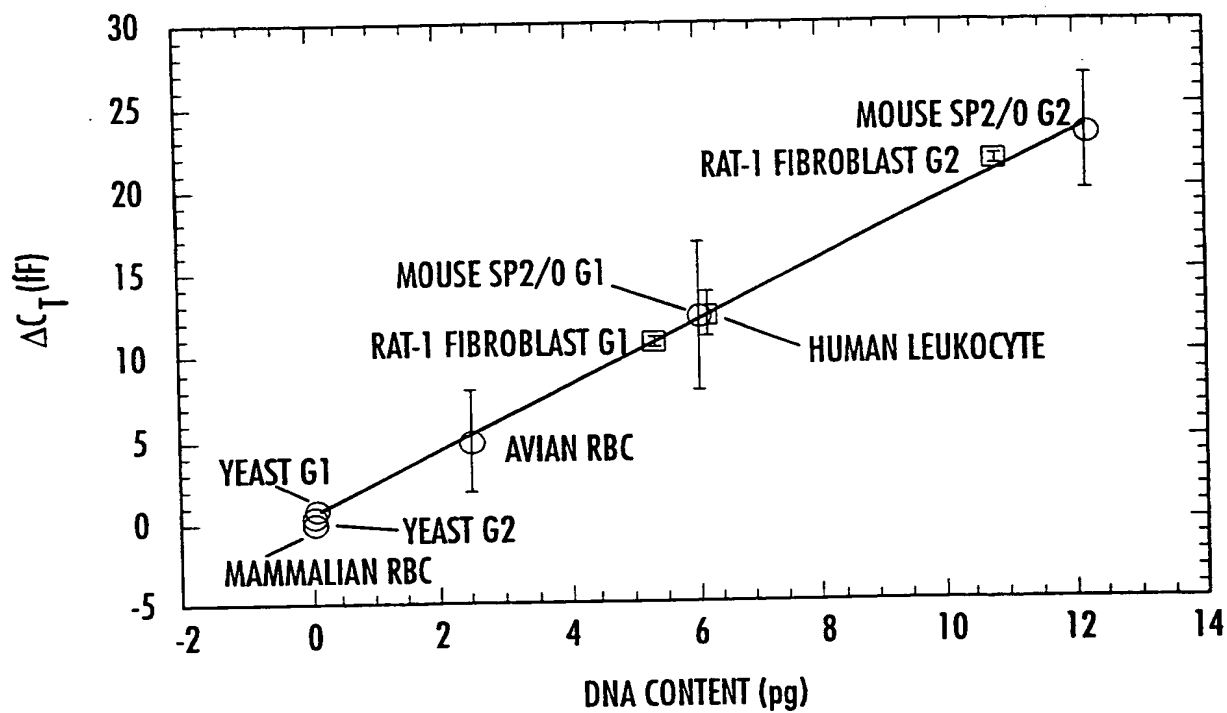
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FIG. 5.

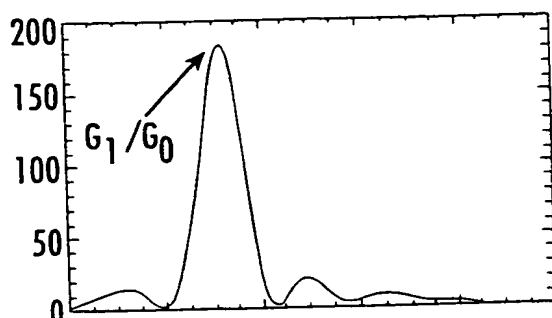
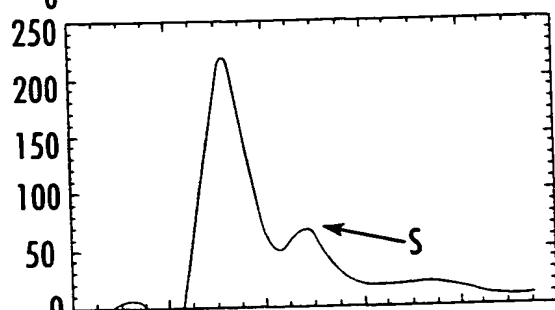
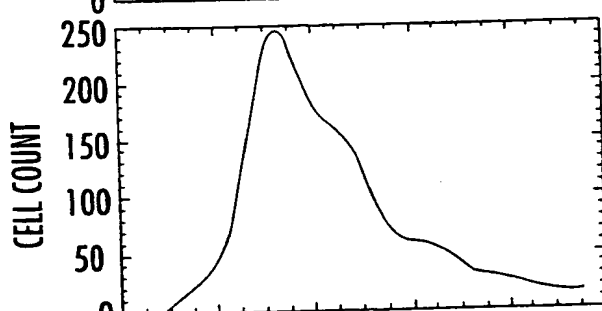
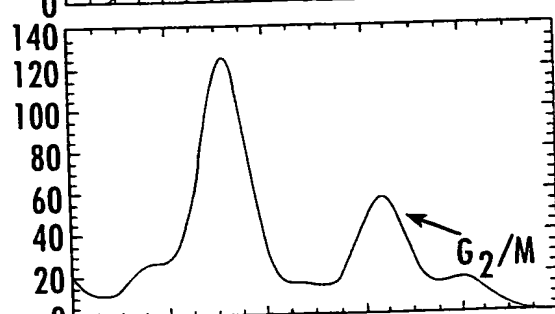
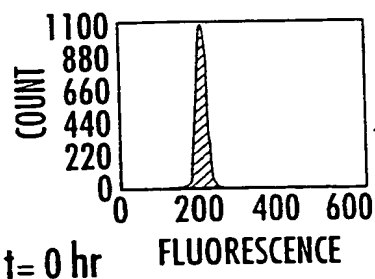
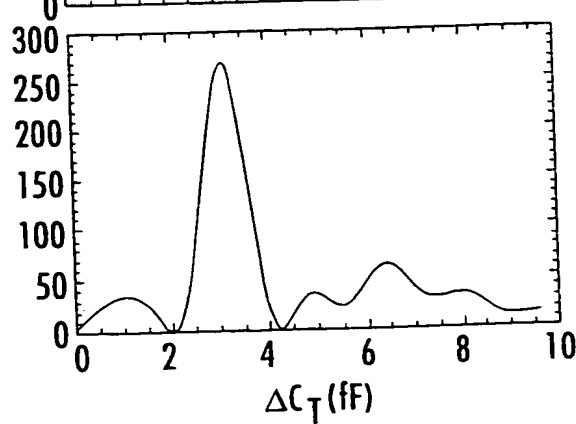
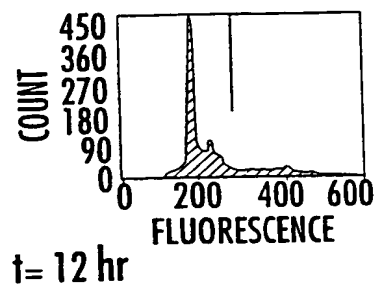
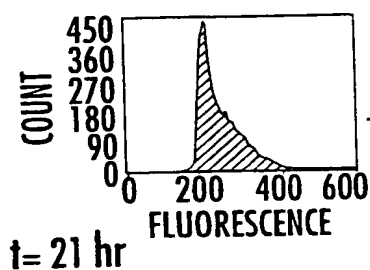
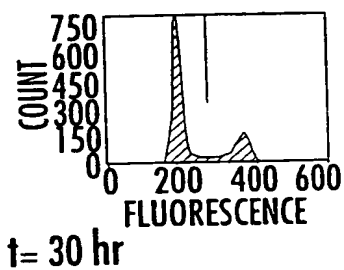
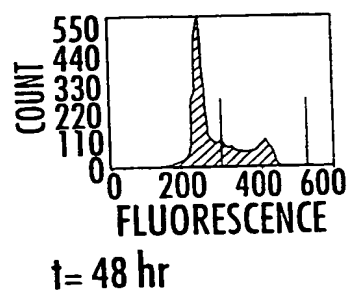
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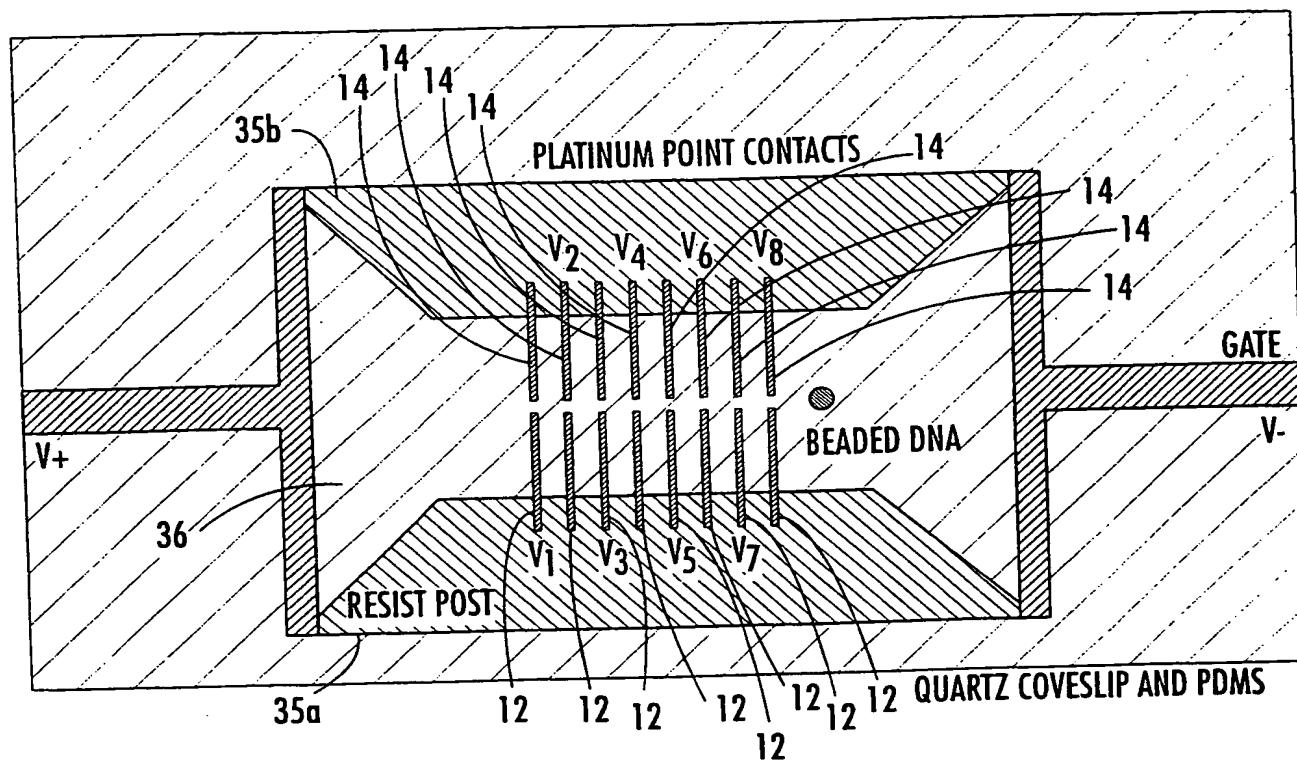
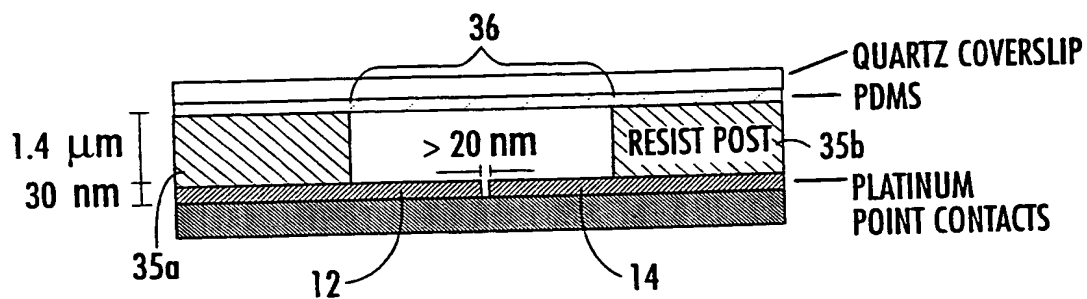
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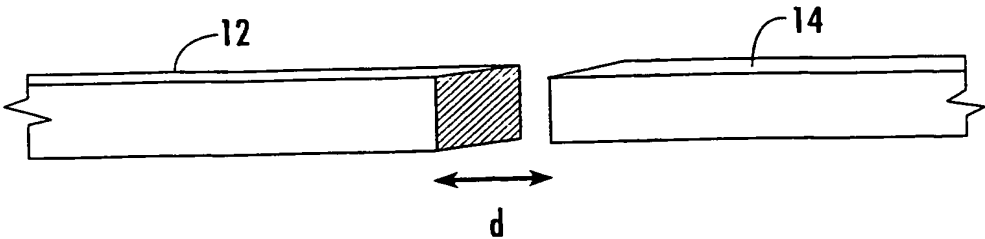
FIG. 7.

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FIG. 8A.FIG. 8B.FIG. 8C.FIG. 8D.FIG. 8E.FIG. 8F.FIG. 8G.FIG. 8H.FIG. 8I.FIG. 8J.

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FIG. 9A.FIG. 9B.



$$C = A\epsilon_0\kappa/d$$

FIG. 10.

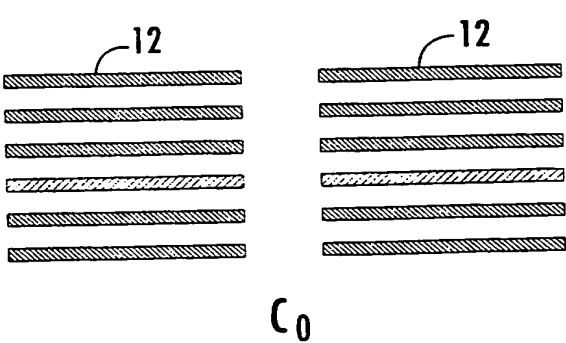


FIG. 11A.

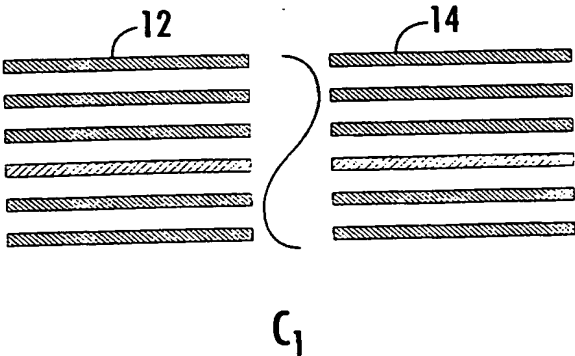
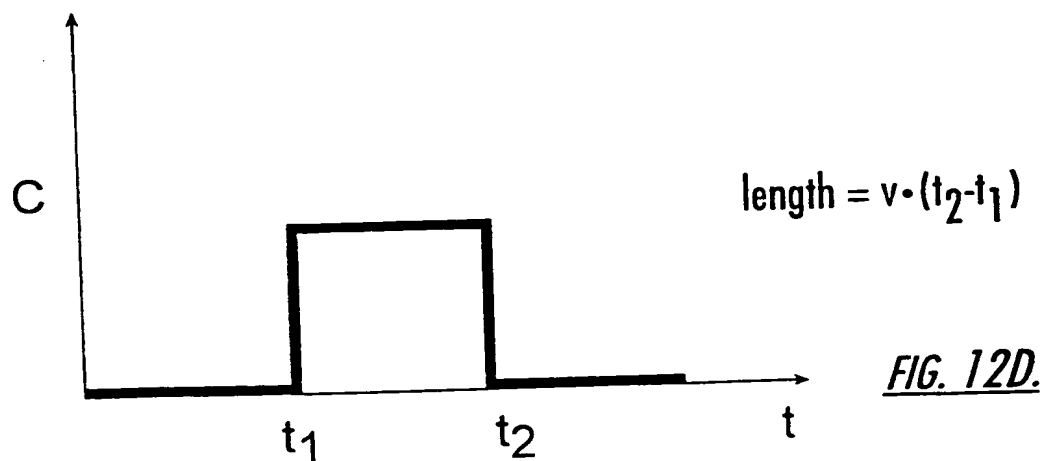
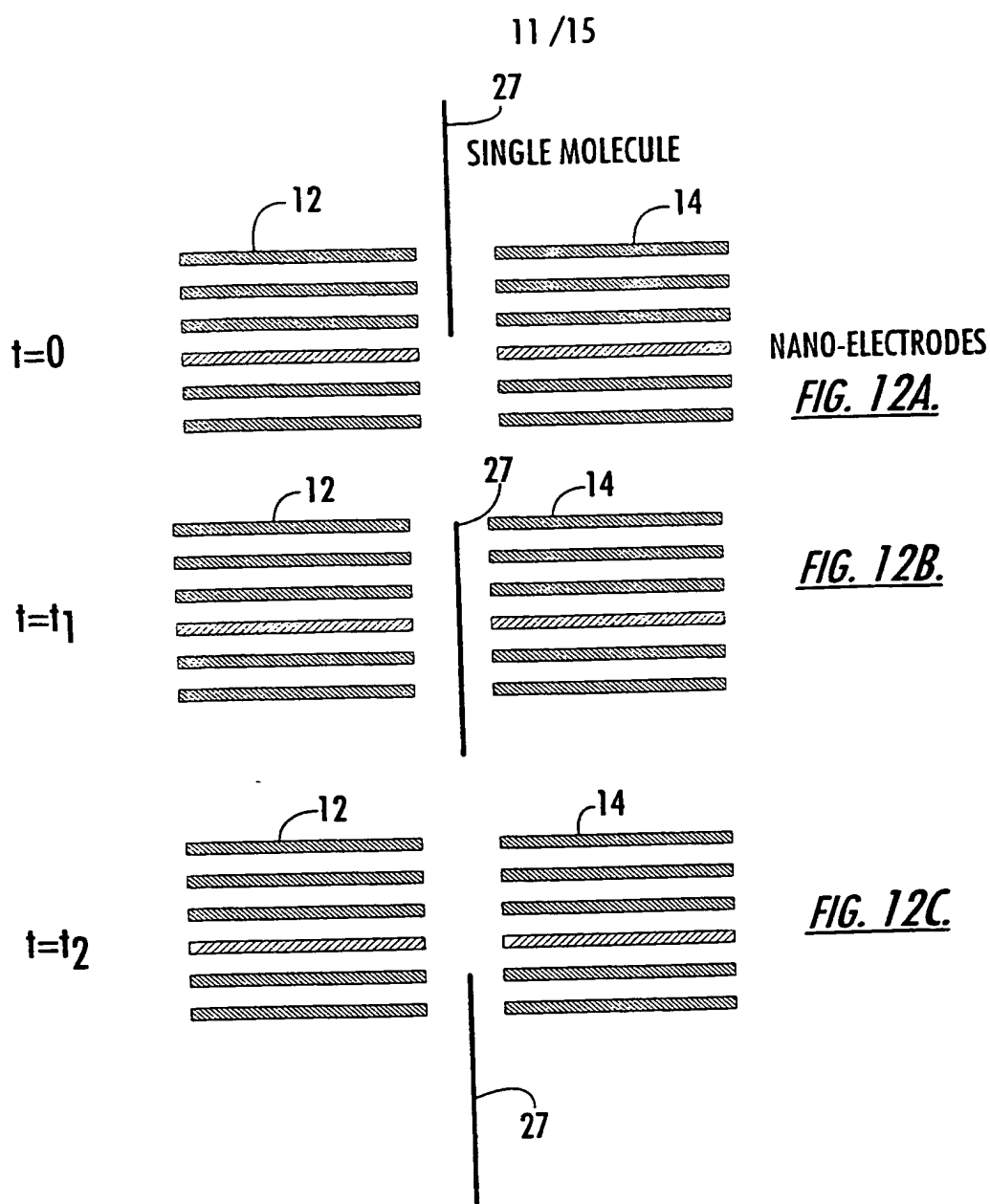


FIG. 11B.



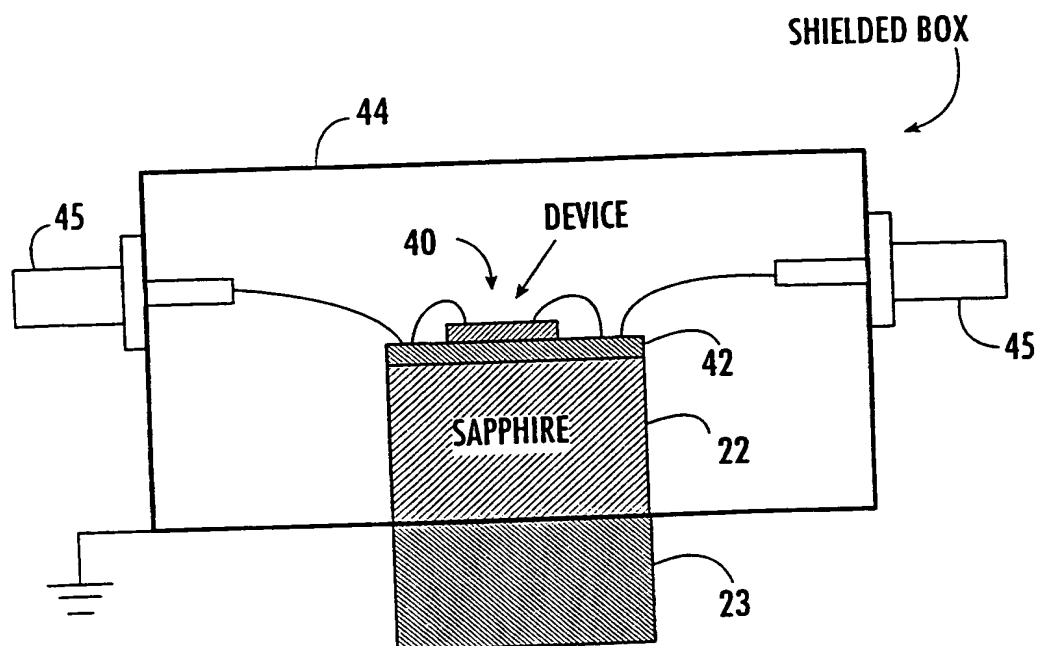
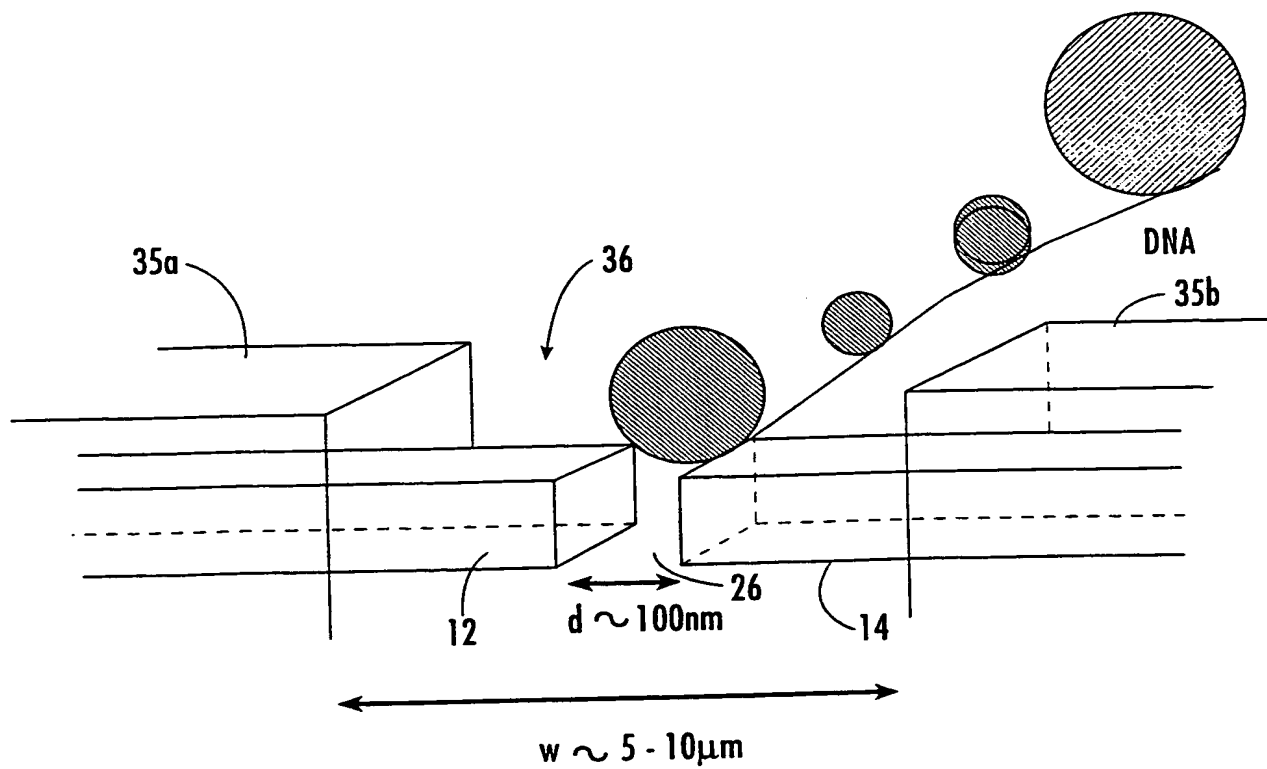
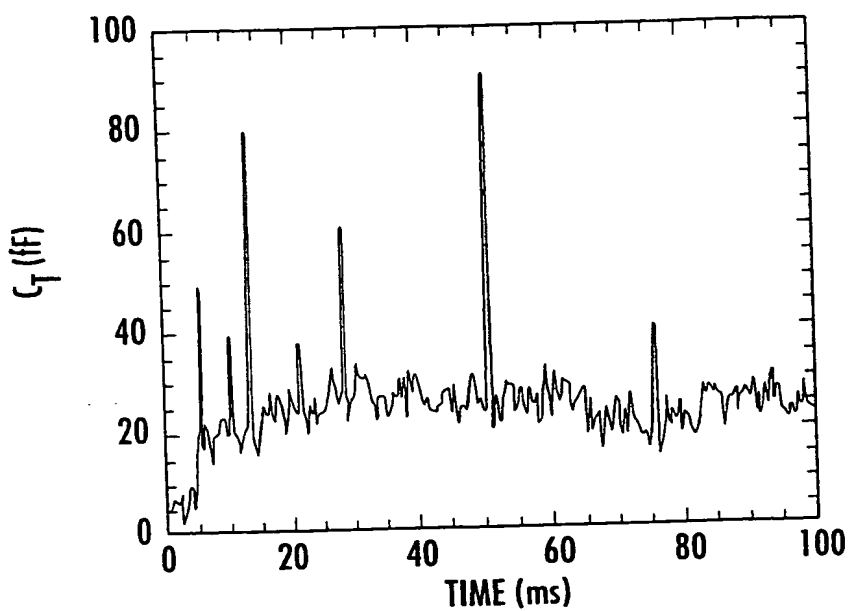
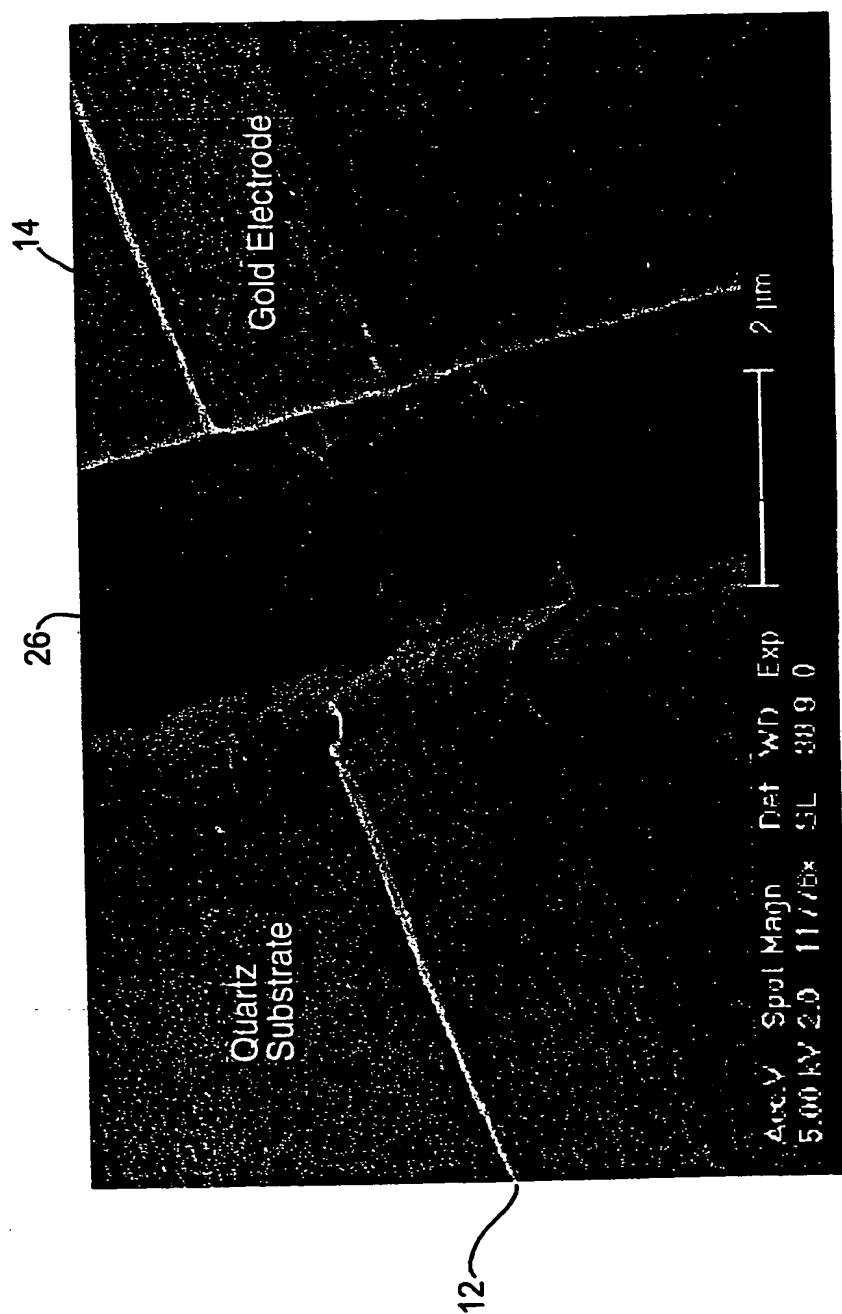


FIG. 13.

**FIG. 14.**

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FIG. 15.

FIG. 16.

INTERNATIONAL SEARCH REPORT

 International application No.
PCT/US00/23652

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : Please See Extra Sheet.

US CL : 435/6, 7.2, 283.1, 285.2; 536/23.1, 25.32, 422/99

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6, 7.2, 283.1, 285.2; 536/23.1, 25.32, 422/99

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----- Y	US 5,744,366 A (KRICKA et al) 28 April 1998 (4/28/98), see entire document especially column 6 lines 49-51, column 8 lines 53-61, column 15 lines 17-27 and column 17 lines 19-25.	1-10, 17-19, 24-27, 34, 35, 37-42, 48, 50, 52, 53-58, 65, 66 & 67 ----- 11-16, 20-23, 28-33, 36, 43-47, 49, 51, 59-64, 68-70



Further documents are listed in the continuation of Box C.



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* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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Date of the actual completion of the international search

04 JANUARY 2001

Date of mailing of the international search report

06 FEB 2001

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4,810,650 A (KELL et al) 07 March 1989 (3/7/1989), see entire document especially column 10 line 11-12).	11-16,20-23, 28-33,36,43-47,49,51, 59-62,69 & 70
Y	US 5,824,477 A (STANLEY) 20 October 1998 (10/20/98), see entire document especially abstract)	65
X ----- Y	WO 94/02846 A1 (BRITISH TECHNOLOGY GROUP LTD) 03 February 1994 (2/3/94), see entire document.	54-56,60,69 & 70 ----- 61 & 62
Y	ASAMI K. et al. Real-Time Monitoring of Yeast Cell Division by Dielectric Spectroscopy. Biophysical Journal. June 1999, vol. 76, pages 3345-3348.	63,64,68

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/23652

A. CLASSIFICATION OF SUBJECT MATTER:

IPC (7):

C12Q 1/68; G01N 33/53; C12M 1/00, 1/42; C07H 21/02, 21/00; B01L 3/00